Chapter 18. Technology and cancer systems: creating better policy to enhance equality

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Summary of key points

- The research agendas of high-income countries have led to a global cancer research effort that is dominated by all things high-tech, whether diagnostic, surgical, radiotherapeutic, or pharmaceutical.
- The benefits of technologies are unevenly distributed between countries and between certain populations (e.g. low-income groups, elderly populations, and ethnic minorities) within countries.
- Research domains essential to improving equality (e.g. prevention, palliative care, health services research, and even childhood cancer) receive little financial or political support, compared with technology-driven models and pathways of care and cultures of clinical practice.
- Policy interventions to manage technologies include: creating a research culture that incentivizes the development of affordable technologies; building pathways and models of care according to evidence-based cancer guidelines; controlling pricing and reimbursements; and engaging the public and patients.
- Weaving clinically meaningful new technologies into cancer care in an affordable and rational manner requires an ethos in national cancer control planning that focuses on systems and better care, not just on innovation and access.

A tsunami of technology

The application of technology – defined as the production or use of advanced or sophisticated tools, whether diagnostic, surgical, radiotherapeutic, or pharmaceutical – in cancer control is a mixed blessing. Its benefit or harm depends on many intrinsic and external factors. In this sense, technology is both a cure for and a cause of global inequalities in cancer. By any metric, cancer is one of the most technocentric global disease domains. Methods developed by Cambrosio et al. (2006) were used to estimate

that, of the total number of publications in the field of cancer (~125 000) in 2017, a staggering 72.6% had some form of technology at their core. This percentage is predicted to rise to 82.6% of about 200 000 publications per year by 2027; many of these will be published by major emerging powers, such as China, which has seen the volume of its technocentric research publications experience a massive 23% compound annual growth rate in the past 10 years (Chinese Journal of Cancer, 2017). The research agendas of high-income countries (HICs) and institutions that wish to industrialize their innovation have led to a global cancer research effort that is dominated by high-tech and rapid technology transfer (Kneller, 2001).

For instance, in the latest review of future cancer research innovations in the USA by a Lancet Oncology Commission, the list of the top 20 consists of some of the most advanced technologies in biomedicine, never mind cancer care (Jaffee et al., 2017). An example is liquid biopsies, which involve the sampling and analysis of non-solid biological tissue as part of an early detection strategy. In addition, artificial intelligence and advanced analytical methodologies have a wide-ranging role, from predicting how cancers will progress and evolve on the basis of their genetic profiles to optimizing chemotherapeutic treatment delivery schedules to reduce toxicity without compromising tumour control. Other technologies include DNA cages, which enable precise delivery of chemotherapy drugs to tumour cells in vivo in response to ultraviolet light, and the genome-editing tool CRISPR/Cas9, which has been used to engineer genomes and to activate or repress the expression of genes. CRISPR/Cas9 provides an efficient technology to dissect mechanisms of tumorigenesis and discover new therapeutic targets (Zhan et al., 2018). Next-generation systemic therapeutics will be aimed at the microbiome, immunome, and epigenome.

The traditional hegemony of pharmaceuticals in this technological space is now being augmented by precision surgery, including the intelligent scalpel (which provides instantaneous diagnosis during surgery), nanorobotics (Felfoul et al., 2016), and radical new applications of computing to radiotherapy planning (e.g. deep learning to facilitate automated treatment contouring and planning). Emerging powers are also joining this global technocentric paradigm at a rapid rate. In a recent review of the 150 most important research questions facing Chinese researchers, 149 were concerned with some form of technology (Chinese Journal of Cancer, 2017). For example, the rapid rise in lung-cancer-specific research in China (which in 2016 overtook the USA to become

the country producing the most research in this field) has been built mostly on technical innovations (Aggarwal et al., 2016).

Technology for cancer control draws from a wide field, from research tools (e.g. sequencing machines) to the primary modalities of treatment (e.g. medicines, surgery, and radiotherapy), supported by the two further domains of imaging and pathology. In 1970 there were 48 cancer medicines used in 102 different regimens; today, a typical health-care system in an HIC has about 746 cancer medicines that can be combined into more than 3540 regimens (Arruebo et al., 2011). Surgery has also undergone rapid technological expansion during the same period. In 1970, 289 instruments were used in 37 procedures with three levels of complexity; today, 4899 instruments are used in more than 300 procedures with six levels of complexity (Purushotham et al., 2012; Sullivan et al., 2015).

In addition, many generic technologies, such as mobile phones and the Internet, form a key component of the cancer pathway, whether used to send money to family members to pay for treatment or by doctors to evaluate images and pathology results. By changing the social determinants of health, these technologies undeniably contribute to better outcomes for cancer patients through both earlier diagnosis and direct care (McKenzie et al., 2016).

This rapid expansion has multiple drivers. Cancer has become a platform for innovation across general science and technology; there are few spheres of technology that cannot be applied to cancer care (Sullivan, 2007). Neoliberal policies that favour the private sector above the public sector have also set national policy agendas (Chapman, 2016). The pillar of wealth creation has towered above health as a human right in most national settings, even those traditionally built on the Bismarckian tradition of welfare and solidarity. The commercial imperative, framed by the World Trade Organization Agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS) and national policies such as the 1980 Bayh–Dole Act in the USA, has also created an ecosystem where technological innovation for profit takes primacy (Boettiger and Bennett, 2006). Revenues from the sales of cancer medicines are expected to reach US$ 147 billion by 2020 (compound annual growth rate, 10%). Pharmaceutical product life-cycles have shortened 5-fold since 1997, and new combinations, treatment stacking (i.e. more treatments added into models of care), and increases in off-label prescribing have been major drivers of increased use.

Technological innovation has also changed the meaning of cancer through advances in cytological, morphological, and genotypic phenotyping; this has created an exponentially increasing number of types of cancers, as well as pathways of care, defined by prognostic stratification (Aparicio and Caldas, 2013). The evolving culture of cancer care, and cancer medicine more broadly, has also played a major part in these changes. The biomedical paradigm includes the use of innovative technology and personalized medicine as key determinants of a good cancer care system (as well as perceived high-quality care), despite the many shortcomings of these developments (Davis and Abraham, 2013; Tannock and Hickman, 2017).

Technology: a cure for and a cause of inequality

The most cursory examination of improvements in cancer outcomes since the 1940s reveals the positive impact of innovative technologies across the spectrum (Nathanson, 1943), from new forms of classic chemotherapy, which can now cure many childhood and adult haematological malignancies, to advances in surgical technologies (e.g. total mesorectal excision), which have dramatically improved rectal cancer mortality rates (Heald and Ryall, 1986; Heald et al., 2017). Indeed, technological improvements in surgery, radiotherapy, pathology, and imaging, linked to earlier diagnosis and better screening (e.g. of cervical cancer), have been the foundations for improved population outcomes. Point-of-care visual inspection with acetic acid (Basu et al., 2015) for cervical cancer screening, targeted at the most vulnerable female populations, is an excellent example of how a technology can directly reduce inequalities in outcomes (Shastri et al., 2014). Other so-called frugal innovations also promise to deliver technological innovations that could, in theory, reduce inequalities by providing diagnostic and pathological tools to rural health centres, thereby improving early diagnosis in these vulnerable populations (Horton et al., 2018; Sayed et al., 2018). For example, a screening device for oral cancer that attaches to a smart phone, lab-on-a-chip devices, and the foldscope (a folding microscope) are all affordable, easy-to-use technologies that can help to deliver pathology services outside major centres (Cybulski et al., 2014; Esfandyarpour et al., 2017).

It is now also clear that many technological developments, such as the ability to transfer funds using mobile phones, have contributed indirectly to better outcomes by enabling patients to access health care. In India, publicly funded second-opinion services such as Navya (https://www.navyanetwork.com/), provided by the National

Cancer Grid of India, have been of huge benefit to patients in groups with lower socioeconomic status (SES) in providing improved access to free public cancer care (Pramesh et al., 2014a). Despite issues related to privacy, the system of digital identity of all Indian citizens (the Aadhaar) is also likely to have a significant positive impact on cancer care by providing a dedicated method of linking insurance and patients with public hospitals (Nilekani, 2011).

However, the benefits of these technologies are unevenly distributed between countries and between certain populations (e.g. low-income groups, elderly populations, and ethnic minorities) within countries. Technologies are embedded within models and pathways of care and cultures of clinical practice. It follows that any health system that is based largely on the power of the market, that fails in its national duties to provide access to high-quality cancer care, and that takes inadequate steps to address the underlying socioeconomic causes of late-stage diagnosis cannot deliver equality in access to cancer technologies.

The focus on pharmaceuticals and biomarkers means that nearly all federal, philanthropic, and private cancer research funders are now aligned in their financial support of expensive cancer treatments (Cambrosio et al., 2006; Aggarwal et al., 2017a). In comparison, research domains that are essential to improving equality (e.g. prevention, palliative care, health services research, and even childhood cancer) receive little support or political capital (Pritchard-Jones et al., 2011; Sullivan et al., 2013); for example, the United Kingdom philanthropic funder Cancer Research UK spends less than 2% of its £700 million annual budget on prevention. This imbalance has led to significant inequalities in outcomes with a global research system focused on expensive medicines for wealthy patients in wealthy countries; such innovations have improved outcomes for those patients but not for patients in groups with lower SES, even in HICs (Aggarwal et al., 2017a). This finding is not limited to HICs but is increasingly being observed in emerging economies, where domestic, affordable innovations are being displaced by high-end expensive technology (e.g. cobalt radiotherapy machines are being displaced by linear accelerator technology) (Sullivan et al., 2014).

Pharmaceuticals represent a paradox in the link between technology and inequalities. Many countries lack basic medicines, resulting in poor outcomes for those patients with cancer types for which medicines are the major modality of cure and

control; however, the creation of a generation of expensive cancer drugs that are delivering less and less clinically meaningful benefit has created both real and perceived inequalities (Del Paggio et al., 2017a, b). The inequality paradox in cancer medicines is highlighted by emerging economies in Europe that are unable to deliver basic chemotherapeutic drugs but are nevertheless putting increasing resources into newer immunotherapies (Cherny et al., 2017).

High-resolution analysis of direct cancer expenditures across Europe has found significant overspend on low-impact clinical technologies and underspend on basic, high-impact clinical technologies, particularly in countries with lower Human Development Index, leading to a complete disconnection between cancer expenditure and outcomes (Luengo-Fernandez et al., 2013, 2016). Such actions have the potential to deliver more harm to the most vulnerable sectors of society, who experience worse outcomes because of the lack of access to basic cancer care, in addition to facing financial toxicity from low-value high-tech care. An emerging issue in all countries is the perception of inequality by patients who, misled by media hype, believe that the latest technologies (e.g. proton beam therapy) provide some miraculous route to cure, irrespective of the clinical facts.

In the past two decades, the Bellwether non-pharmaceutical technology that epitomizes the increasing socioeconomic inequalities as a result of the introduction of new technologies in cancer care has been the da Vinci robotic surgical system. This device, which enables surgeons sitting at a console to operate remotely controlled arms for minimally invasive surgery, was first granted United States Food and Drug Administration approval in 2000. It was expected that its inherent advantages (i.e. improved visualization of the surgical field, enhanced range of motion of the robotic arms, and improved ergonomics for the surgeon) would translate into improvements in patient outcomes (Wright, 2017). However, in the case of prostate cancer and rectal cancer, no improvements in functional or oncological outcomes have been observed (Ilic et al., 2017; Jayne et al., 2017). Despite the lack of clear evidence for its superiority over open and laparoscopic techniques and its higher associated costs, the robotic surgical system has rapidly been implemented across the USA and Europe, and even in many low- and middle-income countries (Barbash and Glied, 2010; Ramsay et al., 2012). It could now be considered the cornerstone of surgical treatment for prostate cancer in these countries, with increasing use across tumour types, despite the lack of

level one evidence (e.g. evidence from at least one properly designed randomized controlled trial) (Kaye et al., 2015; Wright, 2017).

Studies have demonstrated that the uncoordinated adoption of new technologies in health systems has created a socioeconomic differentiation in access to cancer care (Aggarwal et al., 2017b, 2018). In the English National Health Service, where health care is free at the point of use, robotic surgery for prostate cancer has been adopted piecemeal; as a result, a significant number of men who wish to access these treatments have bypassed local centres in favour of alternative centres where the treatment is routinely available. Men who chose preferentially to travel further to centres that offered robotic prostatectomy were on average younger, fitter, and more affluent than those who did not choose to do so (Aggarwal et al., 2018). This tells us that the geographical variation in the availability of new and so-called innovative technologies within health systems means that these are more likely to be accessed by patients with greater financial or physical resources, creating profound inequalities in access and outcomes.

This compounds entrenched socioeconomic differences in care, especially where men with lower SES are unable to attend higher-performing centres because of economic constraints. Furthermore, such patterns of mobility mean that hospitals located in socioeconomically deprived areas with older demographic profiles have to manage far more complex patient cohorts, with subsequent effects on their measured quality and outcomes (Aggarwal et al., 2017c). The substantial levels of patient mobility driven by the differential availability of robotic surgery have led to competition between hospitals to retain their local patients and prevent a loss of income (Aggarwal et al., 2017d). This resulting competition contributed to the closure of 25% of radical prostatectomy centres in the English National Health Service and the widespread adoption of robot-assisted radical prostatectomy.

Technology has a powerful impact in driving patient demand and the configuration of cancer services, not only in unregulated markets in emerging economies but also in HICs with health systems built on equality and solidarity (Pramesh et al., 2014b). Further inequalities in access to treatments and in outcomes may result as the geographical reconfiguration and closure of services is driven by the decisions of fitter, younger, more affluent individuals, rather than by an understanding of the relative needs of the different populations served (Stitzenberg et al., 2009).

Policy interventions to manage technologies

The impact of technology on cancer control depends on industrial and macroeconomic policy, and it remains an open question whether systems and clinical communities have the will or the appetite to embrace different paradigms in relation to national policies. This is especially the case when so much health care is being delivered in pure market economies with unregulated private sectors and underinvested public systems (Bhattacharyya et al., 2017). The impact of this approach is crystal clear: poor, unequal outcomes coupled with catastrophic expenditures, often as a result of accessing unaffordable (and, in many cases, unnecessary) cancer technologies (Kimman et al., 2012).

Current cancer control systems have two intrinsic flaws, which reflect massive political failure at the national and global levels: (i) the failure of policy-makers to ensure universal health coverage or the rational allocation of resources to key modalities and site-specific cancers; and (ii) the ad hoc funding by governments of extensive pharmaceutical technologies or proton beam therapy in the absence of provision of basic radiotherapy or adequate surgical capacity. To rectify these intrinsic flaws, the following policy interventions, aimed broadly at reducing inequalities in access to affordable and necessary cancer technologies as well as addressing technology-induced inequalities, are strongly recommended.

(i) *Build a culture of funding for affordable technologies*: A reorientation of public funding for research that builds on technology domains that are likely to deliver improvements in outcomes, while minimizing inequalities, is required. Examples of research areas that could reduce price as a barrier to access include: repurposing cancer drugs, using reformulations for childhood cancers, developing new forms of radiotherapy technology that require fewer treatment sessions, and improving surgical outcomes by virtual-reality-enhanced surgical training. This reorientation of funding needs to take place at the same time as building momentum in key non-pharmaceutical technological domains (e.g. pathology, surgery, and radiotherapy) as well as creating a policy dialogue to emphasize that such approaches are not second-class technology and medicine. There is also an urgent need for high-income research funders to more actively fund research in low- and middle-income settings (Rodin et al., 2017). Finally, it is imperative that research funding organizations consider a wider range of

research domains beyond pharmaceuticals and biomarkers, such as diagnostics and prevention, to change the epidemiological course of cancer (earlier-stage diagnosis and/or reduced incidence), rather than the continued focus on therapeutics that are delivering ever more marginal gains (Booth et al., 2008; Davis et al., 2017).

(ii) *Governance:* Clinical governance of pathways and models of care built on evidence-based cancer guidelines and even stricter protocols for cancer treatment are necessary. This should also include the regulation of the private-sector technologies, requiring the demonstration of quality and improved outcomes.

(iii) *Pricing and reimbursement*: A wide range of supply- and demand-side policies are needed to manage technologies, with a specific focus on value-based payment systems and health technology assessment programmes for all technologies.

(iv) *Public and patient engagement and regulation of the marketization of cancer care*: A new narrative is necessary to balance the unrelenting mantra calling for personalized medicine and access to everything for everyone. Technology is not a substitute for better governance in the face of clinical and systems failure or a lack of human resources; technology can only enhance, not create, capacity and capability. Framing cancer as a systems problem could help advance the discourse. More radical, however, would be the introduction of policies that legislated against direct-to-consumer and false advertising and regulated the engagement of the clinical community by technology companies.

Conclusions

Fundamentally, weaving clinically meaningful new technologies into cancer care in an affordable and rational manner requires an ethos in national cancer control planning that focuses on systems and better care, not just on innovation and access (Sullivan et al., 2017).

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